

# **EXHIBIT A124**

# Characteristics of Women Who Use Perineal Powders

KARIN A. ROSENBLATT, PhD, WAYNE A. MATHEWS, MS, JANET R. DALING, PhD,  
LYNDA F. VOIGT, PhD, AND KATHLEEN MALONE, PhD

**Objective:** To examine demographic and behavioral factors related to perineal application of powders.

**Methods:** Controls from three case-control studies ( $N = 1206$ ) were asked identical questions about the use of genital powders by direct perineal application. The relationship of perineal powder application with demographic factors, reproductive factors, body mass index (BMI), douching, and alcohol and tobacco use was assessed. Data were analyzed by multiple logistic regression.

**Results:** Women who douched (prevalence odds ratio [prevalence OR] 2.0, 95% confidence interval [CI] 1.0, 3.9), drank alcohol (prevalence OR 1.8, 95% CI 1.2, 2.8), smoked cigarettes (prevalence OR 1.3, 95% CI 1.0, 1.8), or were in the highest BMI quartile were more likely to engage in perineal use of powder (prevalence OR 1.6, 95% CI 1.1, 2.6). There appeared to be a close response relationship between the number of perineal applications of powder and BMI ( $P < .002$ ).

**Conclusion:** Body mass index might confound the relationship between perineal powder application and the development of ovarian cancer. Other factors, such as alcohol and tobacco use and douching, are related to perineal use of powder and may represent similar behavioral characteristics. (Obstet Gynecol 1998;92:753-6. © 1998 by The American College of Obstetricians and Gynecologists.)

The application of powders containing talc to the genital area has been associated with an elevated risk for the development of ovarian cancer in some<sup>1-4</sup> but not all studies<sup>5</sup> that investigated it. In the one study<sup>6</sup> that analyzed it, the authors found that the risk of ovarian cancer increased when women were exposed to increasing applications of genital talc over a lifetime.

Direct perineal application has been the form of

exposure that has been associated most consistently with the development of ovarian cancer.<sup>1</sup> This paper investigates the factors that might be associated with the use of powder in the perineum to identify potential confounding factors that might obscure or exaggerate the association between genital powder exposure and the development of ovarian cancer.

## Materials and Methods

Subjects included in this study were a group of population controls from three case-control studies conducted between 1986 and 1992 from King, Pierce, and Snohomish counties in western Washington (rheumatoid arthritis,<sup>7</sup> breast cancer,<sup>8</sup> and endometrial cancer<sup>9,10</sup>). These women were selected by random-digit dialing using the Waksberg method.<sup>11</sup> To minimize geographic clustering, two residences were selected for each randomized set of telephone numbers. A one-step recruitment method was used with a stratified sampling design.<sup>12,13</sup> This screening procedure was used to identify the age and county of the household members. All telephone numbers were called at least nine times, at different times of the day, during 2 to 6 weeks. Women who refused to take part in the screening procedure were called 4 to 6 months later, and 50% of these were converted to a positive response.

Study subjects who were eligible were sent a letter about the study and were contacted by an interviewer within 3 weeks. Eligibility criteria for study participation included age (39 to 74 years), because these women were at highest risk for the diseases studied; residence in defined three-county area; and ability to communicate in English.

Screening was successful for 93% of the residential numbers. Of 3493 controls that were identified and were determined to be eligible, 712 refused the interview, yielding a response of 79.6%. This yielded an overall response of 76.6%. The data set used in this

From the Department of Community Health, University of Illinois at Urbana-Champaign, Champaign, Illinois; Kirby Hospital, Monticello, Illinois; Fred Hutchinson Cancer Research Center, Southern Illinois University, Carbondale, Illinois; University of Washington School of Public Health and Community Medicine, Seattle, Washington.

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analysis included only the 1697 subjects born before 1944. Of these, 489 were excluded because they had been asked about hysterectomy and were excluded if hysterectomy was performed. In addition, two subjects also were not included in this analysis because they were not asked about talc use. This yielded a total of 1206 subjects for this analysis.

A standardized, in-person interview was administered in all three studies to ascertain information on a wide variety of lifestyles, demographic factors, and medical history data. A calendar of major life events and photographs of oral contraceptives and hormone preparations were used to facilitate recall, and only exposures occurring before a reference date (usually 1 to 2 years before interview) were ascertained in the questionnaires. Women were asked specific questions about direct application to the perineum, including age at first and last use and frequency of use per period of application.

Because the data included in this analysis were cross-sectional in nature, the prevalence odds ratio (OR) was used to compare women who used genital powder with those who did not. Logistic regression analyses using EGRET (Statistics and Epidemiology Research Corporation, Seattle, WA) statistical software were used to estimate the prevalence ORs and 95% confidence intervals (CIs) of the associations of various factors with total talc use and use of powder on the private areas. Prevalence ORs were adjusted for age and other potential confounders such as alcohol use. The relationship with douching was investigated in a subset of the data. The group with perineal powder exposure included women who answered that they "had used powder on their private areas." Trends of the total number of lifetime applications with ordinal variables (including body mass index [BMI], total number of lifetime episodes of douching, and number of sexual partners) were examined using weighted least squares regression analysis of the proportion exposed.<sup>14</sup>

## Results

The proportion of women who had ever applied powder directly to perineal areas (Table 1) decreased with increasing age. A relatively higher proportion of women who used powder in this way also had douched (prevalence OR 2.0, 95% CI 1.0, 3.9), consumed alcohol (prevalence OR 1.8, 95% CI 1.2, 2.8), or smoked cigarettes (prevalence OR 1.3, 95% CI 1.0, 1.8). Women in the highest BMI were relatively more likely ever to have used powder in the perineal area (prevalence OR 1.6, 95% CI 1.1, 2.5). Women with a higher income were less prone to use powder ( $P = .026$ ). There were no consis-

tent associations with education, parity, religious preference, or oral contraceptive use.

Women who had a higher BMI were more prone to have used a greater number of applications of powder on the perineal area over their lifetime ( $P < .002$ ). No trend with dose of powder was seen with number of douching episodes over a lifetime or number of sexual partners (not shown).

## Discussion

We observed several associations that will be compared with previously published literature,<sup>6</sup> and their implications will be discussed. Our findings differ slightly from those of Harlow et al<sup>6</sup> with respect to the age distribution of talc users. We observed a decreasing use with increasing age for perineal application of talc. In contrast, Harlow et al<sup>6</sup> found that use of genital talc increased with increasing age. This may be due to the ethnic, racial, cultural, and demographic characteristics of the study populations and to the possibility of potential reporting bias.

In our study, douching appeared to be related strongly to the use of genital powder. This association is important because douching can cause ascendancy of particles to the ovaries and may increase exposure of genital powder. Several authors have found that infections with sexually transmitted diseases are more common in those who douche, and this may be related to ascendancy of microbial organisms up the vaginal tract (human immunodeficiency virus,<sup>15</sup> sexually transmitted diseases,<sup>16</sup> and pelvic inflammatory disease and chlamydia<sup>17</sup>).

The use of powder on the perineal areas was associated negatively with income. It appears that education and income have at times had a positive association with ovarian cancer, although the association is less apparent recently.<sup>18</sup> The association that perineal powder exposure has with socioeconomic status indicates that socioeconomic status could be a confounder in the relationship between perineal powder exposure and ovarian cancer.

With respect to BMI, there appears to be a relationship with amount of powder use on perineal areas and amount of total genital powder use. This differs from the findings of Harlow et al,<sup>6</sup> who found no association. The relationship that suggests that the more overweight a woman is, the more prone she is to use powder on her private areas could be due to the fact that the more obese a woman is, the more problems she will have with dermatologic conditions in the perineal area.<sup>19</sup> Powder may be used by these women to prevent skin irritation. Although findings are not consistent, some studies have observed that more obese women are at a



**Table 1.** Associations of Various Factors With Powder Exposure of Any Type of Application\*

Factor	Exposed	Unexposed	Percent exposed	Prevalence OR	95% CI
Age (y)					
45-49	61	119	33.9	1.0 <sup>†</sup>	
50-54	91	146	38.4	1.2	0.8, 1.8
55-59	112	165	40.4	1.3	0.9, 2.0
60-64	109	162	40.2	1.3	0.9, 1.9
65-69	49	99	33.1	1.0	0.6, 1.5
70-75	28	65	30.1	0.8	0.5, 1.4
				P = .311 <sup>‡</sup>	
Education					
Grade school	13	29	31.0	1.0	
High school	177	309	36.4	1.3	0.6, 2.6
Technical school	29	54	34.9	1.2	0.6, 2.8
College	180	304	37.2	1.4	0.7, 2.7
Graduate school	51	58	46.8	2.0	1.0, 4.4
Missing	0	2	0.0	P = .099	
Income					
< \$15,000	61	121	33.5	1.0	
\$15,000-\$29,999	149	211	41.4	1.4	0.9, 2.0
\$30,000-\$44,999	101	168	37.6	1.1	0.8, 1.7
≥\$45,000	124	226	35.4	1.0	0.7, 1.5
Missing	15	30	33.3	P = .475	
Religious preference					
None	54	78	40.9	1.1	0.7, 1.6
Catholic	61	161	27.5	0.6	0.4, 0.8
Jewish	7	11	38.9	0.9	0.4, 2.4
Other Christian	315	480	39.6	1.0	
Other	13	25	34.2	0.8	0.4, 1.6
Missing	0	1	0.0		
Parity					
0	39	88	30.7	1.0	
1	42	76	35.6	1.2	0.8, 2.1
2	142	199	41.6	1.6	1.0, 2.5
3	101	170	37.3	1.3	0.8, 2.0
4+	126	223	36.1	1.2	0.8, 1.8
				P = .919	
Number of sex partners					
0	3	14	17.6	0.4	0.1, 1.4
1	215	391	35.5	1.0	
2-4	126	221	36.3	1.0	0.8, 1.4
5-14	81	93	46.6	1.6	1.1, 2.3
15+	22	32	40.7	1.3	0.7, 2.3
Missing	3	5	37.5	P = .028	
Oral contraceptive use					
Nonuser	253	453	35.8	1.0	
Ever use	197	303	39.4	1.2	0.9, 1.6
Duration of use					
1-8 mo	51	75	40.5	1.2	0.8, 1.8
9-35 mo	42	74	36.2	1.1	0.7, 1.6
36-95 mo	62	75	45.3	1.6	1.0, 2.3
96+ mo	42	79	34.7	1.0	0.6, 1.5
				P = .724	
Douching					
Never douched	20	56	26.3	1.0	
Ever douched	137	135	50.4	2.9	1.6, 5.1

**Table 1.** Continued

Factor	Exposed	Unexposed	Percent exposed	Prevalence OR	95% CI
<b>BMI quartile</b>					
1	90	155	36.7	1.0	
2	116	247	32.0	0.8	0.6, 1.1
3	109	182	37.5	1.0	0.7, 1.4
4	132	172	43.4	1.3	0.9, 1.8
Missing	0	3	0.0		<i>P</i> = .029
<b>Alcohol</b>					
Nondrinker <sup>§</sup>	65	185	26.0	1.0	
Drinker	384	568	40.3	2.0	1.4, 2.7
<b>Drinks/wk</b>					
0.001-0.5	90	120	42.9	2.2	1.5, 3.2
0.501-1.5	67	132	33.7	1.5	1.0, 2.2
1.501-5	117	181	39.3	1.9	1.3, 2.7
5.01+	110	135	44.9	2.4	1.6, 3.4
Missing	1	3	25.0		<i>P</i> = .436
<b>Cigarettes</b>					
Nonsmoker <sup>  </sup>	180	369	32.8	1.0 <sup>¶</sup>	
Smoker	270	387	41.1	1.2	1.0, 1.6

OR = odds ratio; CI = confidence interval; BMI = body mass index.

\* Includes those exposed to powder on sanitary napkins, powder to the private areas, (noncornstarch) powder on diaphragms.

<sup>†</sup> Adjusted for age.<sup>‡</sup> Test for trend.<sup>§</sup> ≤4 drinks per year.<sup>||</sup> ≤100 cigarettes in a lifetime.<sup>¶</sup> Adjusted for age and alcohol drinking.

greater risk for ovarian cancer.<sup>20</sup> This suggests that BMI may act as an important confounder of the association between genital talc use and ovarian cancer, but the mechanism by which this might occur is not provided by our data because they are cross-sectional in nature. In addition, our study could have been biased if responders differed from nonresponders in their frequency of powder use.

Our findings also suggest that so-called feminine hygiene practices such as genital powder use and douching could be related and that investigating the reasons for these practices could overlap and may provide insight into potential ways these behaviors could be controlled. Clinicians may want to ascertain information on these practices when obtaining gynecologic history. Future investigations should focus on the motivations for these practices and attempt to determine whether genital talc exposure is causally associated with the development of ovarian cancer. This could be accomplished by behavioral studies of the use of genital powders and additional examinations of the relationship of talc and ovarian cancer.

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Address reprint requests to:

Karin Rosenblatt, PhD

Department of Community Health

University of Illinois at Urbana-Champaign

120 Huff Hall

1206 South Fourth Street

Champaign, IL 61820

E-mail: krosenbl@uiuc.edu

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